| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|---|---|---|---|---|---|---|
| L1 | 29 | Trono NEAR didier | US-PGPUB; USPAT; EPO; JPO; DERWENT | OR | ON | 2004/12/02 17:23 |
| L3 | 4708 | (lentiviral lentivirus HIV$2) WITH vector | US-PGPUB; USPAT; EPO; JPO | OR | ON | 2004/12/02 17:19 |
| L4 | 7218 | (replication NEAR (defective incompitant)) (self NEAR inactivating) | US-PGPUB; USPAT; EPO; JPO | OR | ON | 2004/12/02 17:29 |
| L6 | 1282 | l3 and l4 | US-PGPUB; USPAT; EPO; JPO | OR | ON | 2004/12/02 17:21 |
| L7 | 322 | l3 SAME l4 | US-PGPUB; USPAT; EPO; JPO | OR | ON | 2004/12/02 17:21 |
| L8 | 6144 | hematopoietic ADJ stem ADJ cell | US-PGPUB; USPAT; EPO; JPO; DERWENT | OR | ON | 2004/12/02 17:22 |
| L10 | 99 | l7 and l8 | US-PGPUB; USPAT; EPO; JPO; DERWENT | OR | ON | 2004/12/02 17:22 |
| L11 | 56 | l6 and (delet$5 NEAR LTR) | US-PGPUB; USPAT; EPO; JPO; DERWENT | OR | ON | 2004/12/02 17:24 |
| L12 | 26 | l11 and l8 | US-PGPUB; USPAT; EPO; JPO; DERWENT | OR | ON | 2004/12/02 17:24 |
| L13 | 2345 | EF1$3 NEAR promoter (PGK NEAR promoter) | US-PGPUB; USPAT; EPO; JPO | OR | ON | 2004/12/02 17:26 |
| L14 | 153 | l13 and l6 | US-PGPUB; USPAT; EPO; JPO | OR | ON | 2004/12/02 17:27 |
| L15 | 63 | l14 and l8 | US-PGPUB; USPAT; EPO; JPO | OR | ON | 2004/12/02 17:27 |
| L16 | 13 | l15 and SIN | US-PGPUB; USPAT; EPO; JPO | OR | ON | 2004/12/02 17:29 |

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     (FILE 'HOME' ENTERED AT 17:31:01 ON 02 DEC 2004)

     FILE 'MEDLINE, SCISEARCH, CAPLUS, MEDICONF' ENTERED AT 17:31:50 ON 02 DEC
     2004
L1         34463 S (LENTIVIR? OR HIV? OR RETROVIR?) (L) VECTOR
L2         13056 S (REPLICATION (L) (DEFECTIVE OR INCOMPITANT)) OR (SELF (L) INA
L3          1292 S L1 (L) L2
L4         90500 S HEMATOPOIETIC (L) (STEM OR PROGENITOR OR PRECURSOR) (L) CELL
L5         85862 S HEMATOPOIETIC (S) (STEM OR PROGENITOR OR PRECURSOR) (S) CELL
L6           116 S L3 (L) L5
L7            54 DUP REM L6 (62 DUPLICATES REMOVED)
L8            25 S L7 AND PY<=2000
L9            25 SORT L8 PY
L10            1 S L9 AND SIN
L11          136 S L3 AND SIN
L12           39 S L11 AND L5
L13           17 DUP REM L12 (22 DUPLICATES REMOVED)
L14           17 SORT L13 PY
                 E TRONO DID?/AU
L15          142 S E4
L16            9 S L15 AND L3
L17            8 DUP REM L16 (1 DUPLICATE REMOVED)
L18            8 SORT L17 PY

=> d an ti so au ab pi l18 7

L18  ANSWER 7 OF 8  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:23440  CAPLUS
DN   138:84478
TI   Self-inactivating lentiviral vectors
     for gene therapy capable of driving high level expression of therapeutic
     genes
SO   U.S. Pat. Appl. Publ., 40 pp.
     CODEN: USXXCO
IN   Trono, Didier; Salmon, Patrick
AB   HIV-derived lentivirus vectors which are
     safe, highly efficient, and drive high levels of expression of transgenes
     in human cells for gene therapy, especially, in human hematopoietic progenitor
     cells as well as in all other blood cell derivs. are described.  The
     lentiviral vectors comprise a self-
     inactivating configuration for biosafety.  The vectors
     carry only the gag, pol, and rev genes.  The promoter function of the long
     terminal repeats (LTR) is diminished by inactivation of the U3 region of
     the right LTR.  Promoters such as the EF1α promoter are used to
     drive transgene expression and addnl. promoters are also described.  The
     vectors can also comprise addnl. transcription enhancing elements
     such as the wood chuck hepatitis virus post-transcriptional regulatory
     element.  These vectors therefore provide useful tools for
     genetic treatments such as inherited and acquired lympho-hematol.
     disorders, gene-therapies for cancers especially the hematol. cancers, as well
     as for the study of hematopoiesis via lentivector-mediated modification of
     human HSCs.  Construction of vectors based on HIV-1
     and murine leukemia virus is demonstrated.  Vectors pseudotyped
     with vesicular stomatitis virus G glycoproteins efficiently infected CD34+
     cells.  Efficient expression of reporter genes from PGK and EF1α
     promoters was seen.
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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PI   US 2003008374        A1    20030109    US 2001-10081          20011109

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L18 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:760311 CAPLUS
DN 130:120179
TI **Self-inactivating lentivirus vector** for safe and efficient in vivo gene delivery
SO Journal of Virology (1998), 72(12), 9873-9880
CODEN: JOVIAM; ISSN: 0022-538X
AU Zufferey, Romain; Dull, Thomas; Mandel, Ronald J.; Bukovsky, Anatoly; Quiroz, Dulce; Naldini, Luigi; **Trono, Didier**
AB In vivo transduction of nondividing cells by human immunodeficiency virus type 1 (**HIV**-1)-based **vectors** results in transgene expression that is stable over several months. However, the use of **HIV**-1 **vectors** raises concerns about their safety. Here we describe a **self-inactivating HIV**-1 **vector** with a 400-nucleotide deletion in the 3' long terminal repeat (LTR). The deletion, which includes the TATA box, abolished the LTR promoter activity but die not affect **vector** titers or transgene expression in vitro. The **self-inactivating vector** transduced neurons in vivo as efficiently as a **vector** with full-length LTRs. The inactivation design achieved in this work improves significantly the biosafety of **HIV**-derived **vectors**, as it reduces the likelihood that replication-competent **retroviruses** will originate in the **vector** producer and target cells, and hampers recombination with wild-type **HIV** in an infected host. Moreover, it improves the potential performance of the **vector** by removing LTR sequences previously associated with transcriptional interference and suppression in vivo and by allowing the construction of more-stringent tissue-specific or regulatable **vectors**.

L18 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:816778 CAPLUS
DN 135:14992
TI High-level transgene expression in human hematopoietic progenitors and differentiated blood lineages after transduction with improved lentiviral vectors
SO Blood (2000), 96(10), 3392-3398
CODEN: BLOOAW; ISSN: 0006-4971
AU Salmon, Patrick; Kindler, Vincent; Ducrey, Odile; Chapuis, Bernard; Zubler, Rudolf H.; **Trono, Didier**
AB Recent expts. point to the great value of **lentiviral vectors** for the transduction of human hematopoietic stem cells (hHSCs). **Vectors** used so far, however, have been poorly satisfying in terms of either biosafety or efficiency of transgene expression. Herein is described the results obtained with human immunodeficiency virus-based **vectors** optimized in both of these aspects. It is thus shown that **vectors** containing the EF1α and, to a lesser extent, the phosphoglycerate kinase (PGK) promoter, govern high-level gene expression in human hematopoietic progenitors as well as derived hematopoietic lineages of therapeutic relevance, such as erythrocytes, granulocytes, monocytes, dendritic cells, and megakaryocytes. EF1α promoter-containing **lentiviral vectors** can also induce strong transgene expression in primary T lymphocytes isolated from peripheral blood. A **self-inactivating** design did not affect the performance of EF1α promoter-based **vectors** but significantly reduced expression from the PGK promoter. This neg. effect could nevertheless be largely rescued by inserting the post-transcriptional regulatory element of woodchuck hepatitis virus upstream of the **vector** 3' long terminal repeat. These results have important practical implications for the genetic treatment of lymphohematol. disorders as well as for the study of hematopoiesis via the lentivector-mediated modification of hHSCs.

L18 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:52217 CAPLUS
DN 132:198941
TI **Self-inactivating lentiviral vectors** with enhanced transgene expression as potential gene transfer system in

Parkinson's disease
SO Human Gene Therapy (2000), 11(1), 179-190
CODEN: HGTHE3; ISSN: 1043-0342
AU Deglon, Nicole; Tseng, Jack L.; Bensadoun, Jean-Charles; Zurn, Anne D.; Arsenijevic, Yvan; De Almeida, Luis Pereira; Zufferey, Romain; **Trono, Didier**; Aebischer, Patrick
AB Glial cell line-derived neurotrophic factor (GDNF) is able to protect dopaminergic neurons against various insults and constitutes therefore a promising candidate for the treatment of Parkinson's disease. **Lentiviral vectors** that infect quiescent neuronal cells may allow the localized delivery of GDNF, thus avoiding potential side effects related to the activation of other brain structures. To test this hypothesis in a setting ensuring both maximal biosafety and optimal transgene expression, a **self-inactivating** (SIN) **lentiviral vector** was modified by insertion of the posttranscriptional regulatory element of the woodchuck hepatitis virus, and particles were produced with a multiply attenuated packaging system. After a single injection of 2 μl of a lacZ-expressing **vector** (SIN-W-LacZ) in the substantia nigra of adult rats, an average of 40.1 ± 6.0% of the tyrosine hydroxylase (TH)-pos. neurons were transduced as compared with 5.0 ± 2.1% with the first-generation **lentiviral vector**. Moreover, the SIN-W **vector** expressing GDNF under the control of the mouse phosphoglycerate kinase 1 (PGK) promoter was able to protect nigral dopaminergic neurons after medial forebrain bundle axotomy. Expression of hGDNF in the nanogram range was detected in exts. of mesencephalon of animals injected with an SIN-W-PGK-GDNF **vector**, whereas it was undetectable in animals injected with a control **vector**. **Lentiviral vectors** with enhanced expression and safety features further establish the potential use of these **vectors** for the local delivery of bioactive mols. into defined structures of the central nervous system.

L18 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:282701 CAPLUS
DN 138:298819
TI Restricted expression lentiviral vectors and their gene therapy and related applications
SO PCT Int. Appl., 105 pp.
CODEN: PIXXD2
IN **Trono, Didier**; Wiznerowicz, Maciej
AB The present invention provides **HIV**-derived lentivectors which are safe, highly efficient, and very potent for expressing transgenes for human gene therapy, especially, in human hematopoietic progenitor cells as well as in all other blood cell derivs. The **lentiviral vectors** comprise promoters active to promote expression specific to cell types or tissues. Further, promoters are provided (e.g., from the gp91-phox and CD11b genes) that are amenable to control by activators, enhancers, or repressors. These **vectors** are in a **self-inactivating** configuration for biosafety. Addnl. promoters and hypersensitive sites from the gp91phox promoter are also described. The **vectors** can also comprise addnl. transcription enhancing elements such as the woodchuck hepatitis virus post-transcriptional regulatory element or human hepatitis B virus post-transcriptional regulatory element, without any decrease in the specificity or control exerted by the promoters. These **vectors** therefore provide useful tools for genetic treatments such as inherited and acquired lympho-hematol. disorders, gene therapies for cancers (especially the hematol. cancers), as well as for the study of hematopoiesis via lentivector-mediated modification of human HSCs. **Vectors** are exemplified for gene therapy of chronic granulomatous disease (expression of the gp91-phox subunit of NADPH oxidase) and leukocyte adhesion deficiency (expression of integrin gene under control of the CD11b promoter).

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2003029412 | A2 | 20030410 | WO 2002-US31023 | 20020930 |
| WO 2003029412 | A3 | 20040226 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|
| EP 1438075 | A2 | 20040721 | EP 2002-780402 | 20020930 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| US 2003138954 | A1 | 20030724 | US 2002-261078 | 20021202 |

L18 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:117973 CAPLUS
DN 138:164686
TI Highly contained replication incompetent lentiviral gene therapy vectors and systems for their propagation
SO PCT Int. Appl., 94 pp.
CODEN: PIXXD2
IN **Trono, Didier**; Zufferey, Romain N.
AB **Lentivirus vectors** derived from human immunodeficiency virus that have a number of modifications that make them very safe, efficient, high-level expression **vectors** for gene therapy are described. The modifications include, in combination: an inactive central polypurine tract, a stuffer sequence, which may encode drug susceptibility genes, and a mutated hairpin in the 5' leader sequence that substantially abolishes replication. In addition, genes essential for viral replication are on plasmids containing mutations that prevent replication competent virus being formed by recombination. These elements are provided in conjunction with other features of **lentiviral vectors**, such as a **self-inactivating** configuration for biosafety and promoters such as the EF1α promoter as one example. Addnl. promoters are also described. The **vectors** can also comprise addnl. transcription enhancing elements such as the wood chuck hepatitis virus post-transcriptional regulatory element. These **vectors** therefore provide useful tools for genetic treatments for inherited and acquired disorders, gene-therapies for cancers and other disease, the creation of industrial and exptl. production systems utilizing transformed cells, as well as for the study of basic cellular and genetic processes.

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2003012054 | A2 | 20030213 | WO 2002-US24275 | 20020801 |
| WO 2003012054 | A3 | 20031120 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2003082789 | A1 | 20030501 | US 2002-209952 | 20020801 |
| EP 1412493 | A2 | 20040428 | EP 2002-763401 | 20020801 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |

L18 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:23440 CAPLUS
DN 138:84478
TI **Self-inactivating lentiviral vectors** for gene therapy capable of driving high level expression of therapeutic genes
SO U.S. Pat. Appl. Publ., 40 pp.
CODEN: USXXCO
IN **Trono, Didier**; Salmon, Patrick
AB **HIV**-derived **lentivirus vectors** which are safe, highly efficient, and drive high levels of expression of transgenes

in human cells for gene therapy, especially, in human hematopoietic progenitor cells as well as in all other blood cell derivs. are described. The **lentiviral vectors** comprise a **self-inactivating** configuration for biosafety. The **vectors** carry only the gag, pol, and rev genes. The promoter function of the long terminal repeats (LTR) is diminished by inactivation of the U3 region of the right LTR. Promoters such as the EF1α promoter are used to drive transgene expression and addnl. promoters are also described. The **vectors** can also comprise addnl. transcription enhancing elements such as the wood chuck hepatitis virus post-transcriptional regulatory element. These **vectors** therefore provide useful tools for genetic treatments such as inherited and acquired lympho-hematol. disorders, gene-therapies for cancers especially the hematol. cancers, as well as for the study of hematopoiesis via lentivector-mediated modification of human HSCs. Construction of **vectors** based on **HIV**-1 and murine leukemia virus is demonstrated. **Vectors** pseudotyped with vesicular stomatitis virus G glycoproteins efficiently infected CD34+ cells. Efficient expression of reporter genes from PGK and EF1α promoters was seen.

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2003008374 | A1 | 20030109 | US 2001-10081 | 20011109 |